CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCCAGAGGGTCCCTTG GAAAATGAGGCCAGGGTCCCTGCTGCTGCTTGTTCTGCTGCTCGCCCTGTCCAGGAGCCTGCGGGGCAAA GAGTGTGCGTCTCCACCCTGTGAGTGTCACCAGGAGGACGACTTCAGAGTCACCTGCAAGGAGCTCCACC GAATCCCCAGCCTGCCGCCCAGCACCCAGACTCTGAAGCTCATCGAGACTCATCTGAAGACCATACCCAG TCTTGCATTTTCGAGTCTGCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTG GAACCACATTCTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTAACCT ATATAGACCCTGATGCCTTGACAGAGCTCCCCTTGCTCAAGTTTCTTGGCATTTTCAATACTGGACTTAG AATATTCCCTGACTTGACCAAAATTTATTCCACGGACATATTCTTTATACTTGAAATCACAGACAACCCT TACATGACTTCGGTCCCTGAAAACGCATTCCAGGGCCTATGCAATGAAACCTTGACCCTGAAACTGTACA ACAATGGATTTACTTCAGTCCAAGGACATGCTTTCAATGGAACAAAGCTGGATGCTGTTTACCTAAACAA GAATAAATACCTGACAGCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGAT GTGTCTTCCACCAGCGTCACTGCCCTTCCTTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCAAAAG ${\tt ACACCTGGACTCTCAAAAAGCTCCCGCTGTCGTTGAGTTTCCTCCACCTCACTCGGGCTGACCTCTCTTA}$ CCCGAGCCACTGCTGCGCTTTTAAGAACCAGAAGAAAATCAGGGGAATCCTGGAGTCTTTGATGTGTAAT GAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCAGTGAACATCTTGAGGGGTCCCATCTACCAGGAAT $\verb|CTCTCACTATTACGTCTTCTTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAAT| \\$ CCTCAGGAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGGACAACGAGGACA TGGTGTGTACCCCCAAGTCGGACGAGTTTAACCCCTGTGAAGATATCATGGGCTACAGGTTCCTGAGAAT $\tt CGTGGTGTGGTTTGTCAGTCTGCTGGCTCTCCTGGGCAATATCTTCGTCCTGCTCATTCTGCTAACCAGC$ ${\tt CACTACAAATTGACCGTGCCGCGGTTCCTCATGTGCAACTTGGCCTTTGCAGATTTCTGCATGGGGGTAT}$ ACCTGCTTCTCATTGCCTCTGTAGACCTGTACACACACTCTGAGTACTACAACCACGCCATCGACTGGCA GACGGGCCCTGGGTGCAACACGGCTGGCTTCTTCACTGTTTTCGCCAGTGAGTTATCAGTGTACACACTG ACGGTCATCACCCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGCCTCA GGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCCTGCTTCTTCTCGCCCTGCTCCCGATGGTGGG AATCAGCAGCTATGCCAAGGTCAGCATCTGCCTGCCAATGGACACCGACACCCCTCTTGCACTCGCATAC ${\tt ATTGTCCTCGTTCTGCTGAATGTTGTTGCCTTTTGTTGTCGTCTGTTCCTGCTATGTGAAGATCTACA}$ ${\tt TCACGGTCCGAAATCCCCAGTACAACCCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTTT}$ GATCTTCACTGACTTCATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTCGGCACTTATGAACAAGCCT $\tt CTAATCACTGTTACTAACTCCAAAATCTTGTTGGTTCTCTTCTACCCCCTCAACTCCTGTGCCAATCCGT$ TTCTCTATGCTATTTTCACCAAGGCCTTCCAGAGGGACGTGTTCATCCTGCTCAGCAAGTTTGGCATCTG CAAACGCCAGGCCCAGGCCTATCAGGGTCAGAGAGTCTGTCCCAACAATAGCACTGGTATTCAGATCCAA AAGATTCCCCAGGACACGAGGCAGAGTCTCCCCAACATGCAAGATACCTATGAACTGCTTGGAAACTCCC AGCTAGCTCCAAAACTGCAGGGACAAATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAAGGAAAGGCTA ACATAGGTTCATGCAGGTGATGATTCATAGGGTCAGAGTTCATCTCTAGAAAGTATTGCCTC (SEQ ID NO:1)

FIGURE 1A

MRPGSLLLLVLLLALSRSLRGKECASPPCECHQEDDFRVTCKELHRIPSLPPSTQTLKLIETHLKTIPSLAFSSLPN ISRIYLSIDATLQRLEPHSFYNLSKMTHIEIRNTRSLTYIDPDALTELPLLKFLGIFNTGLRIFPDLTKIYSTDIFF ILEITDNPYMTSVPENAFQGLCNETLTLKLYNNGFTSVQGHAFNGTKLDAVYLNKNKYLTAIDNDAFGGVYSGPTLL DVSSTSVTALPSKGLEHLKELIAKDTWTLKKLPLSLSFLHLTRADLSYPSHCCAFKNQKKIRGILESLMCNESSIRN LRQRKSVNILRGPIYQEYEEDPGDNSVGYKQNSKFQESPSNSHYYVFFEEQEDEVVGFGQELKNPQEETLQAFESHY DYTVCGDNEDMVCTPKSDEFNPCEDIMGYRFLRIVVWFVSLLALLGNIFVLLILLTSHYKLTVPRFLMCNLAFADFC MGVYLLLIASVDLYTHSEYYNHAIDWQTGPGCNTAGFFTVFASELSVYTLTVITLERWYAITFAMRLDRKIRLRHAY TIMAGGWVSCFLLALLPMVGISSYAKVSICLPMDTDTPLALAYIVLVLLLNVVAFVVVCSCYVKIYITVRNPQYNPR DKDTKIAKRMAVLIFTDFMCMAPISFYALSALMNKPLITVTNSKILLVLFYPLNSCANPFLYAIFTKAFQRDVFILL SKFGICKRQAQAYQGQRVCPNNSTGIQIQKIPQDTRQSLPNMQDTYELLGNSQLAPKLQGQISEEYKQTAL (SEQ ID NO:2)

FIGURE 1B

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCCAG AGGGTCCCTTGGAAAATGAGGCCAGGGTCCC] TGCTGCTGCTTGTTCTGCTGCTCCCCT GTCCAGGAGCCTGCGGGGCAAAGAGTGTGCGTCTCCACCCTGTGA ACGACTTCAGAGTCACCTGCAAGGAGCTCCACCGAATCCCCAGCCTGCCGCCCAGCACCC AGACTCT] GAAGCTCATCGAGACTCATCTGAAGACCATACCCAGTCTTGCATTTTCGAGT CTGCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTGGAACCA CATTCTTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTA ACCTATATAGACCCTGATGCCTTGACAGAGCTCCCCTTGCTCAAGTTTCTTGGCATTTTC AATACTGGACTTAGAATATTCCCTGACTTGACCAAAATTTATTCCACGGACATATTCTTT ATACTTGAAATCACAGACAACCCTTACATGACTTCGGTCCCTGAAAACGCATTCCAGGGC CTATGCAATGAAACCTTGACCCTGAAACTGTACAACAATGGATTTACTTCAGTCCAAGGA GCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGATGTGTCT TCCACCAGCGTCACTGCCCTTCCTTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCA AAAGACACCTGGACTCTCAAAAAGCTCCCGCTGTCGTTGAGTTTCCTCCACCTCACTCGG GCTGACCTCTCTTACCCGAGCCACTGCTGCGCTTTTAAGAACCAGAAGAAAATCAGGGGA ATCCTGGAGTCTTTGATGTGTAATGAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCA GTGAACATCTTGAGGGGTCCCATCTACCAGGAATATGAAGAAGATCCGGGTGACAACAGT GTTGGGTACAAACAAAACTCCAAGTTCCAGGAGAGCCCAAGCAACTCTCACTATTACGTC TTCTTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAATCCTCAG GAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGACAACGAG GACATGGTGTACCCCCAAGTCGGACGAGTTTAACCCCTGTGAAGATATCATGGGCTAC AGGTTCCTGAGAATCGTGGTGTGGTTTGTCAGTCTGCTGGCTCTCCTGGGCAATATCTTC GTCCTGCTCATTCTGCTAACCAGCCACTACAAATTGACCGTGCCGCGGTTCCTCATGTGC AACTTGGCCTTTGCAGATTTCTGCATGGGGGGTATACCTGCTTCTCATTGCCTCTGTAGAC CTGTACACACTCTGAGTACTACAACCACGCCATCGACTGGCAGACGGGCCCTGGGTGC AACACGGCTGGCTTCTTCACTGTTTTCGCCAGTGAGTTATCAGTGTACACACTGACGGTC ATCACCCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGC CTCAGGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCCTGCTTCTCTCGCCCTG GACACCCCTCTTGCACTCGCATACATTGTCCTCGTTCTGCTGCTCAATGTTGTTGCCTTT GTTGTCGTCTGTTCCTGCTATGTGAAGATCTACATCACGGTCCGAAATCCCCAGTACAAC CCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTGTTGATCTTCACTGACTTC ATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTCGGCACTTATGAACAAGCCTCTAATC ACTGTTACTAACTCCAAAATCTTGTTGGTTCTCTTCTACCCCCTCAACTCCTGTGCCAAT CCGTTTCTCTATGCTATTTTCACCAAGGCCTTCCAGAGGGACGTGTTCATCCTGCTCAGC AAGTTTGGCATCTGCAAACGCCAGGCCCAGGCCTATCAGGGTCAGAGAGTCTGTCCCAAC AATAGCACTGGTATTCAGATCCAAAAGATTCCCCAGGACACGAGGCAGAGTCTCCCCAAC ATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAAGGAAAGGCTACGCTAGTCACAGTGAG ACTTACAAAAGGCTGGTTTCTTGAACATGCGTTCCAGTCCCGTGACATGTGAACACATAG GTTCATGCAGGTGATGATTCATAGGGTCAGAGTTCATCTCTAGAAAGTATTGCCTC

FIGURE 2A

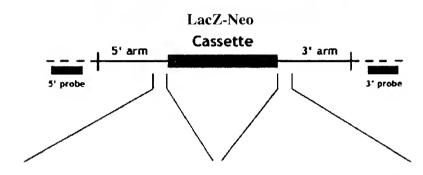
Gene Sequence Structure 91 bp Sequence Deleted 163 bp Size of full-length cDNA: 2512 bp

Targeting Vector* (genomic sequence)

Arm Length: 5': 5 kb 3': 1.3 kb

----- Targeting Vector
------ Endogenous Locus

* Not drawn to scale



	Testes +	Epididymis	Weight	(5)	(8)			0.224										0.076
	Heart/	Body	Weight	8	0 601	0.719	0.795	0 0	0.00	0.555	0.570	0.499	0.610	0.0	24.0	204.0	0.478	42 0.520
		Heart	Weight) (E	0 155	0.155	0 110	0.13	5 6	0.12	0.137	0.045	0.051	0.053	0.000	0.00	0.060	0.042
	Thymus/	Body	Weight	(%)	0.367	0.354	0.224	0.265	0.250	1000	0.258	0.111	0.048	0.266	2000	0.4.0	0.279	0.012
		mus	ight	(E)	8	090	055	993	80	000	.062	010	007	034	34	0 1	.035	.001
	Liver/ Kidney/	Body	Weight	(%)	1.464	1.297	1 393	1 278	1 052	100	1.339	1.219	1.316	1.091	1 142		1.164	1.177
		Kidney	Weight	(6)	0.327	0.220	0.342	0.304	0.238	0.000	0.322	0.110	0.110	0.127	0 134		0.146	0.095
	Liver/	Body	Weight	(%)	5.622	5.307	5.654	5.010	5 624		5.591	4.819	4.569	5.034	5.676		6.202	4.535
		Liver	Weight	(b)	1.256	0.900	1.388	1.192	1272		1.344	0.435	0.382	0.586	0.666	0770	0.778	0.366
	Spleen/	Body	Weight	(%)	0.425	0.307	0.281	0.340	0.354	0000	0.300	0.089	0.191	0.137	0.153	404	<u> </u>	0.087
		Spleen	Weight	(b)	0.095	0.052	0.069	0.081	0.080	0.070	2.0.0	0.008	0.016	0.016	0.018	7000	0.024	0.007
		Body	Weight	(a)	22.339	16.960	24.550	23.792	22.619	24 040	7.040	9.026	8.360	11.640	11.733	12 5AE	12.343	8.070
			_		9	8.25	9.5	9.7	8.5	σ	ס	7.5	7	80	9.7	α	0	^
		((Age Lengtr	(days)	48	48	48	48	48	48	·	47	48	48	48	48	?	48
		,000	cencer		Female	Female	Maie	Male	Female	Male		Female	Female	Female	Male	Male		Male
				-	+/+	+	+/+	+/+	+/-	+		- -	+-	+	-/-	-/-		'

				ı		10) ~	_	_	. ~
			(c)				0.387	•		0.389
Heart/	Bodv	Weight	8	0.5756	0.4826	0.3975	0.4717	0.5572	0.4343	0.4038
	Heart	Weight) (B)	0.145	0.136	0.219	0.201	0 109	0.111	0.102
Thymus/	Body	Veight	· (%)	0.1548	0.1526	0.1343	0.1220	0.2045	0.0978	0.1069
	Thymus	Weight) (B)	0.039	0.043	0.074	0.052	0.040	4 0.025	0.027
Kidney/	Body	Weight	(%)	1.4013	1.3591	1.2598	1.1382	0.9406	5 0.340 1.3304	1.1717
	Kidney	Weight	(B)	0.353	0.383	0.694	0.485	0.184	0.340	0.296
Liver/	Body	/eigh	%	.859	.1348	.930	.0313	.4118	454	.8767
	Liver	Weight	(g)	1.476	1.447	3.267	2.144	0.863	1.394 5	1.232
	Body	Weight	(%)	0.881	0.3228	0.330	0.3192	0.1534	0.3013	0.2019
	Spleen	Weight	(6)	0.222	0.091	0.182	0.136	0.030	0.077	0.051
	Body	Weight	(g)	25.191	28.180	55.089	42.613	19.561	25.557	25.263
		Length	(cm)	9.5	9.918	11.025	1	7.978	307 9.47 2	9.5
	Age at	Test								
		Gender Test Length		Female	Female	Male	Male	Female	-/- Male	Male
				+ /+	+/+	+/+	+/+	-/-	- /-	' -